

LETTERS TO THE EDITOR

Scope

Heart welcomes letters commenting on papers published in the journal in the previous six months. Topics not related to papers published earlier in the journal may be introduced as a letter: letters reporting original data may be sent for peer review.

Presentation

Letters should be:

- not more than 600 words and six references in length
- typed in double spacing (fax copies and paper copy only)
- signed by all authors

They may contain short tables or a small figure. **Please send a copy of your letter on disk.** Full instructions to authors appear in the July 1998 issue of *Heart* (page 104).

Arterial remodelling and eccentricity of plaque

SIR,—We read with interest the article by von Birgelen and colleagues in which they found both vessel and plaque volume in lesions with inadequate compensatory enlargement to be smaller than in lesions with adequate compensatory enlargement.¹ They also found that the eccentricity index (EI)—calculated as minimum wall thickness divided by maximum wall thickness—was higher in lesions with inadequate remodelling than in those with adequate remodelling. Because endothelium dependent arterial dilatation, which has been proposed as a possible mechanism for arterial compensatory remodelling,² requires a normally functioning endothelium, the higher eccentricity produced by a thick wall with plaque and a thin plaque free wall in lesions with adequate remodelling may support that hypothesis as mentioned by Varnava.³ The EI, however, would decrease in relation to the plaque enlargement with an increase in the maximum thickness even if the amount of plaque free endothelium is unchanged. The assumptions that both arterial contour and luminal contour are true circles lead to the following equations.

$$(1) P + L = \pi \times [(D_{\min} + D_{\max} + D_{\text{lum}})/2]^2$$

where P is plaque area, L is luminal area, D_{\min} is minimum wall thickness, D_{\max} is maximum wall thickness, and D_{lum} is luminal diameter.

$$(2) L = \pi \times [D_{\text{lum}}/2]^2$$

$$(3) EI = D_{\min}/D_{\max}$$

Finally, the equation,

$$D_{\min} = 2 \times EI \times [(P+L)^{1/2} - L^{1/2}]/[\pi^{1/2} \times (EI + 1)],$$

can be obtained from equations (1), (2) and (3).

For example, lesion A with $L = 2.4 \text{ mm}^2$, $P = 10.9 \text{ mm}^2$, and $EI = 0.28$ has a D_{\min} of 0.518 mm; lesion B with $L = 2.3 \text{ mm}^2$, $P = 15.2 \text{ mm}^2$, and $EI = 0.21$ has a D_{\min} of 0.522 mm. Although the EI of lesion B is smaller than that of lesion A, the calculated values of D_{\min} are comparable. Therefore, a smaller value of EI does not warrant the larger amount of preserved, normally func-

tioning endothelium. These values used for lesions A and B are the mean values in lesions with adequate and inadequate remodelling, respectively, in the study of von Birgelen *et al.*

We proposed another hypothesis of mechanical deformation to explain arterial remodelling.⁴ This suggests that a larger length of plaque along the cross sectional wall may make a larger luminal enlargement. Although precise methods to determine the ratio of plaque to plaque free endothelium have not been established, Blank and Yeung, who proposed new indices for the ratio of the length of plaque to that of the cross sectional wall, found that a larger plaque produces a higher degree of arterial remodelling when the cross sectional plaque area is less than 55% of the total vessel area.⁵ Because adequate arterial remodelling occurs in the early stage of atherosclerosis,² this observation supports the mechanical deformation hypothesis. We believe more sophisticated methods than calculating the EI for determination of eccentricity are required to assess the mechanism causing arterial remodelling.

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- 1 Von Birgelen C, Mintz GS, de Vreya EA, *et al.* Atherosclerotic coronary lesions with inadequate compensatory enlargement have smaller plaque and vessel volumes: observations with three dimensional intravascular ultrasound in vivo. *Heart* 1998;79:137-42.
- 2 Glagov S, Weisenberg E, Zarins CK, *et al.* Compensatory enlargement of human atherosclerotic coronary arteries. *N Engl J Med* 1987;316:1371-5.
- 3 Varnava A. Coronary artery remodelling. *Heart* 1998;79:109-10.
- 4 Oniki T, Iwakami M. Is arterial remodelling truly a compensatory biological reaction? A mechanical deformation hypothesis. *Atherosclerosis* 1997;132:115-18.
- 5 Blank RD, Yeung AC. Effect of atherosclerotic plaque topography on coronary artery remodelling: an intravascular ultrasound study [abstract]. *J Am Coll Cardiol* 1997;(suppl A):125A.

This letter was shown to the authors, who reply as follows:

We thank Dr Oniki for his thoughtful and interesting comments on his work. We agree that the EI may decrease in relation to plaque enlargement (that is, an increase in maximum plaque thickness) even if the extent of plaque free, cross sectional area, and possibly normal functioning overlying endothelium is unchanged.

Indeed the EI is not a suitable parameter to characterise the presence and extent of plaque free endothelium. However, that was not the idea underlying the use of the EI in our paper. Rather we used the EI to define the eccentricity of plaque distribution. There appeared to be a significant difference between lesions with adequate compensatory enlargement and those with inadequate adaptive remodelling, suggesting that more concentric lesions in that phase of the disease had less compensatory enlargement.

We appreciate the suggestions that the disease free endothelial wall may play a role in the ability of the arterial wall to enlarge and to attract our attention to the hypothesis of mechanical deformation.

Bifid T waves induced by isoprenaline in a patient with Brugada syndrome

SIR,—Washizuka *et al* describe a patient with syncope, believed to have Brugada syndrome, who developed bifid T waves when given isoprenaline.¹ The three ECGs reproduced in their figs 1 and 3, however, fail to show either incomplete or complete right bundle branch block, a hallmark and sine qua non characteristic of the Brugada syndrome. In addition, there is no significant ST segment elevation in lead V1, and the ST segment elevation in V2 is not at all coved-type. The characteristics of Brugada syndrome—right bundle branch block, ST segment elevation, and sudden cardiac death—are all missing.² I am afraid that by injudiciously extending the scope of the Brugada syndrome to include a variety of non-specific electrocardiographic findings in patients who present with syncope, we will see this fascinating entity itself succumb to sudden death.

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- 1 Washizuka T, Chinushi M, Niwano S, *et al.* Bifid T waves induced by isoprenaline in a patient with Brugada syndrome. *Heart* 1998;79:305-7.
- 2 Brugada J, Brugada P. Further characterization of the syndrome of right bundle branch block, ST segment elevation, and sudden cardiac death. *J Cardiovasc Electrophysiol* 1997;8:325-31.

This letter was shown to the authors, who reply as follows:

The ECG of Brugada syndrome characterised by right bundle branch block and persistent ST elevation is known to show day to day variation. The ECG of our patient recorded on another day showed prominent coved-type ST elevation. Class IA drugs accentuated the magnitude of ST elevation, the patient had a history of unexplained syncope, and ventricular fibrillation was induced during electrophysiological study.

As pointed out by Littmann it is difficult to diagnose Brugada syndrome from ECG recordings; however, ECG pattern changes from time to time and the administration of intravenous class IA drugs may unmask the ECG pattern¹ as in our case. In addition, it was suggested that a prominent J wave was part of the ECG abnormality.^{2,3} So a clear diagnosis may be difficult from single ECG recording and we should be careful of diagnosis of Brugada syndrome.

- 1 Brugada J, Brugada P. Further characterization of the syndrome of right bundle branch block, ST segment elevation and sudden cardiac death. *J Cardiovasc Electrophysiol* 1997;8:325-31.
- 2 Bjerregaard P, Gussak I, Kotar SL. Recurrent syncope in a patient with prominent J-wave. *Am Heart J* 1994;127:1426-30.
- 3 Yan GX, Antzelevitch C. Cellular basis for the electrocardiographic J wave. *Circulation* 1996;93:372-9.

Nocturnal desaturation in patients with stable heart failure

SIR,—Staniforth *et al* correctly pointed out that arterial desaturation is common in patients with congestive heart failure, especially while sleeping.¹ The desaturation is commonly associated with apnoeic pauses, presumably as a result of depression of

the respiratory centres (Cheyne-Stokes episodes). However, the seriousness of this depression requires emphasis.

Nocturnal desaturation in obstructive sleep apnoea has been associated with increased severity of hypertension, congestive heart failure, angina pectoris, atrial fibrillation, complete heart block, and possibly precipitation of myocardial infarction. Cerebral blood flow is reduced with the anoxia of obstructive sleep apnoea.² Platelet aggregation and activation are increased two- and threefold.³ These changes are normalised with improved oxygenation. Vgontazs and colleagues⁴ and Entzian and colleagues⁵ identified severely increased inflammatory cytokines, and tumour necrosis factor α and interleukin 6 with anoxia.

Staniforth *et al* stated that "only 4% of their subjects were obstructive and no subject fulfilled the diagnostic criteria for obstructive sleep apnoea." However only 41 (of 104) patients had polysomnography. One wonders about the other patients. Mechanical obstruction should be treated mechanically. The authors emphasise beautifully the serious desaturation that occurs in congestive heart failure, but the need for appropriate treatment gets short shrift.

It appears that all congestive heart failure patients should have nocturnal saturation determined and, if low, properly treated (with supplemental oxygen). Polysomnography is warranted in all who are anoxic with oxygen supplementation. If anoxia is present and oxygen does not correct it, and if an obstructive cause is discovered, continuous positive airway pressure or partial resection of the tongue (where it obstructs the palate) may be helpful.⁶ The surgery is relatively minor and well tolerated. Weight reduction for the obese is an ideal rarely realised; 20–30% of patients with obstructive sleep apnoea are not obese. Snoring without apnoeic periods may be the only sign of inadequate ventilation.

Most patients with congestive heart failure are hospitalised at some time. As part of their evaluation, documentation of nocturnal oxygen saturation would be worthwhile. If anoxemia is present, the effect of oxygen supplementation could be recorded and failure to oxygenate properly would suggest a mechanical obstruction. Polysomnography could be done to document the need for mechanical relief (with continuous positive airway pressure, weight reduction, or surgery). If oxygen treatment alone relieves the anoxia, then clearly the patient should be given oxygen at home. The effects of anoxemia are so pernicious that we should not be constrained to withhold oxygen if the levels are borderline.

One wonders if the brain damage manifested by the Cheyne-Stokes breathing pattern is not a result of chronic anoxia. I am not sure we know the lowest safe level of cerebral

oxygenation. Hopefully, these techniques will improve the very bleak outlook for the congestive heart failure patient.

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- 1 Staniforth AD, Kinnear WJM, Starling R, *et al*. Nocturnal desaturation in patients with stable heart failure. *Heart* 1998;79:394–9.
- 2 Balfors EM, Franklin KA. Impairment of cerebral perfusion during obstructive sleep apnoea. *Am J Resp Crit Care Med* 1994;150:1587–91.
- 3 Bokinsky G, Miller M, Ault K, *et al*. Spontaneous platelet activation and aggregation during obstructive sleep apnoea and its response to therapy with nasal continuous positive airway pressure. *Chest* 1995;108:625–30.
- 4 Vgontazs AND, Papanicolaou DA, Bixler EO, *et al*. Elevation of plasma cytokines in disorders of excessive daytime sleepiness: role of sleep disturbance and obesity. *J Clin Endocrinol Metab* 1997;82:1313–16.
- 5 Entzian P, Linnemann K, Schlaak M, *et al*. Obstructive sleep apnoea syndrome and circadian rhythms of hormones and cytokines. *Am J Resp Crit Care Med* 1996;153:1080–6.
- 6 Straith R E, Ritter G. Partial resection of the tongue for amelioration of obstructive sleep apnoea: a report on 34 cases with long term follow-up. *J Craniomaxillofac Surg* 1997;25:305–9.

This letter was shown to the authors, who reply as follows:

The harmful effects of obstructive sleep apnoea are well documented and are summarised in the letter by Ritter. What is poorly recognised, especially in the UK, is the role of central sleep apnoea (Cheyne-Stokes respiration) as an independent marker of poor prognosis in heart failure.¹ The mechanism behind this is unclear, but our results did not support a causal link between apnoea associated nocturnal desaturation and serious ventricular dysrhythmia. It may be related to activation of the sympathetic nervous system, and we have recently reported the beneficial effects of oxygen treatment on Cheyne-Stokes respiration and sympathetic activation in heart failure.²

We accept the criticism that only 41 of our 104 subjects underwent sleep studies. Polysomnography is the gold standard test for diagnosing sleep apnoea, but it is expensive and for that reason we used it only in a representative subgroup of our patients. These studies identified around 3100 apnoeas, 96% of which were central in origin, and no patient met the standard diagnostic criteria for obstructive sleep apnoea. The total number of events we examined was large, and consequently we do not feel that the quality of our data has suffered. Cheynes-Stokes respiration is common in patients with stable controlled heart failure; prevalences of 27–51% are reported in the literature.^{3,4} We documented a prevalence of 22%. Our study

shows that obstructive sleep apnoea is an unlikely cause of nocturnal desaturation in heart failure patients who do not have a history of pulmonary disease. In this setting, overnight pulse oximetry is an effective screening tool for Cheyne-Stokes respiration. It is important to screen patients with heart failure for Cheyne-Stokes respiration on prognostic grounds. To avoid overdiagnosis, however, the best time to do this may be following discharge when they are clinically stable, rather than during a hospital admission as Ritter suggests. The major advantages of oximetry over polysomnography as a home screening tool are that it is cheap, easily portable, and widely available.

We did not discuss the possible treatment strategies for Cheyne-Stokes respiration in heart failure as the main thrust of our paper was to establish its prevalence, and to demonstrate the usefulness of oximetry as a screening tool. Oxygen, carbon dioxide, continuous positive airway pressure, aminophylline, and sedatives have all been advocated. The advantage of one treatment modality over another remains to be proved, as indeed does the existence of a survival benefit from treating Cheyne-Stokes respiration in heart failure.

- 1 Hanly PJ, Zuberi-Khokhar NS. Increased mortality associated with Cheyne Stokes respiration in patients with congestive heart failure. *Am J Resp Crit Care Med* 1996;153:272–6.
- 2 Staniforth AD, Kinnear WJM, Starling R, *et al*. Effect of oxygen on sleep quality, cognitive function and sympathetic activity in patients with chronic heart failure and Cheyne-Stokes respiration. *Eur Heart J* 1998;19:922–8.
- 3 Blackshear JL, Kaplan J, Thompson RC, *et al*. Nocturnal dyspnea and atrial fibrillation predict Cheyne-Stokes respirations in patients with congestive heart failure. *Arch Intern Med* 1995;155:1297–1302.
- 4 Javaheri S, Parker TJ, Liming JD, *et al*. Sleep apnea in 81 ambulatory male patients with stable heart failure. *Circulation* 1998;97:2154–9.

CORRECTION

Can C reactive protein or troponins T and I predict outcome in patients with intractable unstable angina? N P Curzen et al. Heart 1998;80:22–7.

The C reactive protein data in the results section should have been: mean 17.1 mg/l, median 8.7 mg/l (range 4.8–203.9) and not as published. The median value for C reactive protein in the abstract should have been 8.7 mg/l and not as published.

These errors are regretted; however, they should not affect interpretation of the data or conclusions.